Claims

1. A method for producing a classification scheme for AML comprising the steps of:

a) providing a plurality of reference samples, said reference samples comprising cell samples from a plurality of reference subjects affected by AML;

b) providing reference profiles by establishing a gene expression profile for each of said reference samples individually;

c) clustering said individual reference profiles according to a statistical procedure, comprising:

(i) K-means clustering;

(ii) hierarchical clustering; and

(iii) Pearson correlation coefficient analysis; and

d) assigning an AML class to each cluster.

2. Method according to claim 1, wherein the clustering of said gene expression profiles is performed based on the information of differentially-expressed genes.

3. Method according to claim 1 or 2, wherein the clustering of said gene expression profiles is performed based on the information of the genes of Table 1, more preferably of Table 2.

4. A method for classifying the AML of an AML affected subject, comprising the steps of:

a) providing a classification scheme for AML by producing such a scheme according to the method of any one of claims 1-3;

b) providing a subject profile by establishing a gene expression profile for said subject;

c) clustering the subject profile together with reference profiles;

d) determining in said scheme the clustered position of said subject profile among the reference profiles, and

e) assigning to said AML of said subject the AML class that corresponds to said clustered position in case said subject profile is within any cluster of reference profiles, or assigning to said AML of said subject a new AML class.

5. A method for diagnosing AML in a subject comprising the steps of:

a) producing a classification scheme for AML according to the method of any one of claims 1-3;

b) defining cluster-specific genes for each cluster by selecting those genes of which the expression level characterizes the clustered position of the corresponding AML class among the various AML classes within said scheme;

c) determining the level of expression of one or more of said cluster-specific genes in a subject;

d) establishing whether the level of expression of said cluster-specific genes in said subject shares sufficient similarity to the level of expression that characterizes an individual AML class to thereby determine the presence of AML corresponding to said class in said subject.

6. Method according to claim 5, wherein said cluster-specific genes comprise a set of 1 to 3000 genes of the genes of table 1, more preferably 1 to 600 genes of the genes of table 1, still more preferably 1 to 50 genes of the genes of table 1.

7. Method according to claim 5, wherein said cluster-specific genes comprise a set of 1 to 600 genes of the genes of table 2, still more preferably 1 to 50 genes of the genes of table 2, and even more preferably 1 to 25 genes of the genes of table 2.

8. Method according to claim 5, wherein said cluster-specific genes are selected from the genes of Table 3.

9. A method of determining the prognosis for an AML affected subject, said method comprising the steps of:

a) providing a classification scheme for AML by producing such a scheme according to the method of any one of claims 1-3;

b) determining the prognosis for each AML class in said scheme based on clinical records for the AML subjects comprised in said class;

c) establishing the AML class of an AML affected subject by diagnosing AML in said subject according to any one of the methods 5-8 or by classifying the AML in said subject according to a method of claim 4, and

d) assigning to said subject the prognosis corresponding to the established AML class of said AML affected subject.

10. A method of determining the prognosis for an AML affected subject, said method comprising the steps of:

a) isolation of RNA from mononuclear cells of said subject;

b) preparation of antisense, biotinylated RNA to the RNA of step a);

c) hybridisation of said antisense, biotinylated DNA on Affymetrix U133A or U133 Plus2.0 GeneChips®;

d) normalising the measured values for the gene set of Table 1;

e) clustering the obtained data together with the reference data, obtainable from (www.ncbi.nlm.nih.gov/geo, accession number GSE1159); and

f) determining the prognosis on basis of the subgroup/cluster to which the data of the subject are clustering.

11. Classification scheme for AML, said scheme comprising a plurality of distinct AML classes that are differentiated on the basis of similarity clustering of gene expression profiles obtained from a plurality of reference subjects affected by AML.

12. A method of detecting an AML-associated transcript in a cell from a patient, the method comprising contacting a biological sample from the patient with a polynucleotide that selectively hybridizes to a sequence at least 80%, preferably at least 95% identical to a sequence as shown in Table 1, 2 or 3.

13. Method according to claim 12, wherein said polynucleotide selectively hybridizes to a sequence at least 95% identical to a sequence as shown in Table 1, 2 or 3.

14. Method according to claim 12, wherein said polynucleotide comprises a sequence as shown in Tables 1 or 2.

15. Method according to any one of claims 12-14, wherein said biological sample is a tissue sample.

16. Method according to any one of claims 12-15, wherein the biological sample comprises isolated nucleic acids, e.g., mRNA.

17. Method according to any one of claims 12-16, wherein the polynucleotide is labeled, e.g., with a fluorescent label.

18. Method according to any one of claims 12-17, wherein the polynucleotide is immobilized on a solid surface.

19. Oligonucleotide probe capable of hybridizing under stringent conditions to one or more of the AML-associated genes selected from Table 1, preferably to one or more of the genes selected from Table 2, more preferably to one or more of the genes selected from Table 3.

20. Oligonucleotide microarray comprising at least 1, preferably at least 2, more preferably at least 25, still more preferably at least 100 oligonucleotide probes according to claim 19.

21. Kit-of-parts comprising an oligonucleotide microarray according to claim 20 and means for comparing a gene expression profile determined by using said microarray with a database of AML reference expression profiles.